**REMARKS**

1. General Remarks

1.1. We note that the Petition Decision mailed April 23, 2010 advises that the reference to the February 5, 2010 action as "final" in the office action summary is a typographical error, and that said action is deemed "non-final".

1.2. We note that the February 5, 2010 action examined and rejected the previously unelected claims of groups II (16, 18-20, 22-26, 29, 31-32, 34-35, 37-38, 40-42), III (50-52, 55, 58-59), IV (63-66, 68-76, 79-82, 84-88, 90-93), and V (94-95, 98-100) on written description grounds (office action p. 9) and for some claims on indefiniteness grounds (p. 10), so plainly the restriction requirement has been withdrawn. However, this was not explicitly stated in the February 5 action. In view of the examination of these claims, we have marked them "original", "previously presented" or "currently amended", as appropriate, in the claim listing, rather than as "withdrawn".

1.3. Claim 1 has been limited to Oenococcus oeni, which necessitated cancellation of claims 2, 82, 104, 108, 109 and adjustment of the dependency of 110. 65 has been cancelled as superfluous.

1.4. Method-of-making claim 50 has been rewritten in independent form. New claims 112-113 limit it to oenococcus and Oenococcus Oeni, respectively. Formerly claims 53-54 have been "reinstated" as 114-115[1].

2. Objections (OA p. 2-3)

[1] Since one would not normally speak of "incubating" an organism with a radiation-type mutagenizing agent, claims 114-115 explicitly require a chemical agent

2.1. The examiner identifies the following as trademarks:

"Lallemand" (P37)

"Viniflora (P46, P47, P50)

"Oxoid" P42-45, 47).

"Lallemand" appears in the context of "Lallemand Inc" and thus is clearly non-trademark usage, i.e., it is part of a company name, serving to identify the company from whom the organism was purchased, not a trademark for the microbial organism. For the distinction between a trademark and a trade name, see Trademark Manual of Examining Procedure 1201.01, 1213.03(c) and (d).

"Viniflora" appears to be a scientific genus name, not a trademark.

"Oxoid" appears at P42, L25 in the context of "Oxoid Ltd", and thus is clearly part of a company name. The same is true of the other uses of Oxoid. These are not trademark usages.

2.2. The Examiner objects to claim 65 as failing to further limit the base claim. Claim 65 was previously withdrawn from examination, hence not addressed by us. Since claim 65 is ultimately dependent on claim 1, and claim 1 requires malolactic fermentation activity, claim 65 has been cancelled as superfluous.

3. Definiteness Issues (OA p. 10-11)

3.1. "essentially complete degradation" (claim 1) -- the term "essentially" is not necessarily indefinite, see In re Marosi, and we clearly explained what we meant by the term, see p. 27, lines 1-5 of the last response, citing P15, L13-16.

The issue is moot as claim 1 has been amended to require degradation of malic acid to a level not exceeding 30 mg/L, with basis at P15, L13-16.

3.2. "said grape juice" (claim 34). The antecedent basis problem has been corrected by amending 34 to first recite that the liquid composition is a grape juice or fermented grape juice.

3.3. Previously withdrawn claim 50 is rejected for alleged lack of correlation between the body steps and the preamble purpose. This alleged disconnect occurred because base claim 1 was amended to have additional limitations. We have done so. Arguably, claim 50 is still acceptable because it is open in form ("comprises"). However, we may reasonably amend 50 to require selection for all of the functional limitations of the organism of claim 1, i.e., by updating claim 50 to reflect the second paragraph of claim 1.

3.4. The rejection of "Oenococcus family" and "Lactobacillus family" (claims 66 and 82) as improper family terms is moot in view of the limitation of claim 1 to Oenococcus oeni and cancellation of claims of broader scope.

We note for the record that Lactobacillus is a genus within the family Lactobacillaceae, and Oenococcus is a genus within the family Leuconostocaceae.

3.5. The examiner insists that the term "concentration" (claim 79) is limited to solute in a solution. However, it can refer more generally to the amount of a component of a mixture (even a dry mixture) relative to the amount of the mixture, with the amounts expressed as weights and/or volumes.

Thus, Hawley, The Condensed Chemical Dictionary ($9^{th}$ ed. 1977) states that "concentration" is "the amount of a given substance in a stated unit of a mixture, solution or ore. Common methods of stating concentration are percent by weight

or by volume; … or weight per unit volume…." (P. 224) (Exhibit 2). Note that a "mixture" is defined as "a heterogeneous association of substances, which may or may not be uniformly dispersed". (P. 584). We trust that it is clear that the mixture may be of dry solids.

McGraw-Hill Encyclopedia of Science & Technology, vol. 4 (9th ed. 2002) refers to "concentration scales" as being "numerical systems defining the quantitative relations of the components of mixtures" (P. 584) (Exhibit 3). The remainder of the discussion relates to solutions, but it is clear that the term "concentration" has a broader application.

We respectfully submit that the art would plainly accept the use of term "concentration" to refer as does claim 74 to a "glucose concentration" as being a ratio of glucose by weight to the volume of the dry activation solution of claim 74.

In any event the examiner does not explain what term he would use in claim 79 in lieu of "concentration".

3.6. The examiner questions antecedent basis for "the fermentable compound" in previously withdrawn claim 80. The rejection is well taken.

Original claim 63, directed to an activation solution, required as element iii) a particular amount of "a microbial organism capable of fermenting at least one fermentable compound". Claim 64 required that this compound be malic acid.

Claim 74 of the application as set forth in the May 17, 2006 preliminary amendment likewise recited "a microbial organism capable of fermenting at least one fermentable compound", and the instant claim 80 required that this compound be malic acid.

The quoted limitation was stricken when claims 63 and 74 were amended to depend from claim 1, as claim 1 required

malolactic fermentation, i.e., required that the organism be capable of fermenting malic acid.

It follows that not only claim 80, but also claim 64, are superfluous.

It also appears that claim 81 is superfluous because claim 1 requires that the organism be capable of degrading 1,000-10,000 mg/L malic acid down to 30 mg/L, which is a conversion of at least 97% of the malic acid. Hence, 81 is cancelled.

3.7. Finally, 107 questions the correlation between the body of claim 107 and the preamble. This is similar to the issue raised with regard to claim 50.

However, while 50 was a method claim, 107 is a dependent organism claim. It thus inherently includes all limitations of base claim 1. Claim 107 is open in form and it is not necessary that it recite all of the steps needed to arrive at the organism.

4. Written Description Issues

4.1. Claim 105 stands rejected for alleged lack of written description for "wherein the organism is selected from the group consisting of DSM15569, DSM15570, DSM15571, and mutants derived directly or indirectly therefrom" (OA page 10).

Since P26, L31 discloses that the starting microbial organism to be subjected to mutation is an Oenococcus oeni strain, and the only specifically disclosed strains are those set forth on P37, and include DSM 15569-71, we have possession of the concept of further mutation of DSM 15569-71.

4.2. All claims stand rejected for alleged lack of written description for the claim 1 language, "within the

period required for essentially complete degradation of the malic acid within the medium".

While the amended claim 1 terminology "essentially complete degradation of the malic acid within the medium" is new, the examiner errs in stating that applicant failed to cite basis. There is extensive discussion of the teachings concerning malic acid degradation at pp. 24-27 of the November 5, 2009 amendment, including citation to original claim 8 ("capable of degrading at least 90% of said malic acid"), P16, L27-30 (initial malic acid content, point (11) on page 26 of the amendment), P17, 12-20 (minimum malic acid degradation expressed as final concentration, point (15) thereof), and P15, L22-32, (degradation as %, points (5) and (6) thereof).

Also, note that on page 27, lines 1-5 of that amendment we explain that "essentially complete" in the claim is considered to be when the fermentation is defined by the specification "to be completed", i.e., the malic acid level is not more than 30 mg/L, citing P15, L13-16.

Our concern was that if claim 1 recited that the malolactic fermentation was "complete", that the reader might overlook the special definition of "complete" at P15, L13-16. Hence, we used the language "essentially" complete. In view of the examiner's concerns, we now instead recite explicitly "30 mg/L", with clear basis at P15, L15. New claim 116 recites 15 mg/L, with basis in the same passage.

4.3. Finally, claims 1, 2, 4, 6-8, 11, 16, 18-20, 22-26, 29, 31-32, 34-35, 37-38, 40-43, 45, 48-49, 55, 58-59, 63-66, 70-76, 79-82, 86-88, 90-95 and 98-110 stand rejected for alleged lack of written description for the claimed "genus" (in the legal sense) of organisms.

In claim 1, these were organisms with particular metabolic characteristics that belonged to the genera

*Lactobacillus*, *Pediococcus*, or *Oenococcus*. Dependent claims limited the "genus" to (1) just *Oenococcus* and *Lactobacillus* (claim 82), (2) just *Oenococcus* (claims 104, 108) (3) *Oenococcus oeni* (claims 2, 109), (4) three deposited strains and mutants thereof (claim 105), and (5) organisms obtainable (claim 106) or obtained (claim 107-110) by a particular process, and there were also (6) Markush group claims (not rejected on the instant ground) to the three deposited strains (claims 15, 68, 84).

4.3.1. In the January 7, 2009 office action, page 6, the examiner questioned whether DSM15569, 15570, and 15571 met the limitations of the claim. More precisely, the examiner conceded that "example 4 shows that DSM15569, 15570, and 15571 are capable of the required survival rate," but argued that based on example 2 this would be true only under specific culture conditions and that the claim did not expressly require those conditions.

In our May 4, 2009 response, pages 22-23 we pointed out:

> The claims are directed to the organisms, and not to the method of cultivating the organisms.
>
> Example 2 shows that under some conditions, the organism will have the stated survival rate. It is quite common in microbiology patent claims to recite that an organism is capable of a particular level of performance. Whether it actually achieves that performance is almost certainly dependent on the growth conditions. However, in a claim directed to the organism, it should not be necessary to specify those growth conditions (unless that is necessary to distinguish it from a prior art organism which achieves that performance under less desirable growth conditions).
>
> Reciting the specific growth conditions in the claims would make it much more difficult to prove infringement, because of the difficulties

> of ascertaining the growth conditions used by a potential infringer.
>
> We have amended claim 1 to require that the organism is capable of adaptation to the recited growth rates under "suitable growth conditions". Hence, it is only necessary to show that growth conditions exist in which DSM 15569, 15570 and 15571 are adapted to the recited growth rate, which is already conceded by the examiner.

In the August 13, 2009 rejection, page 6, the examiner states, "applicant is admitting that the only portion of the invention that has been reduced to practice are the strains DSM15569, 15570, and 15571". It does not appear that the examiner then still questioned that those three strains were reduced to practice, and are within the scope of the claim, and hence are "described" for purposes of 35 USC 112, para. 1. If it did, we note that the instant April 23, 2010 action explicitly states that the three deposited strains are "described", see action page 7, line 1.

Consistent therewith, it does not appear that this written description rejection has been applied to claims 15, 68 and 84, which are Markush group claims to just those three strains. For the same reason, this rejection ought not be applied to new claim 111.

Since three strains within the scope of the claim were reduced to practice, the invention is clearly not a mere "research plan".

4.3.2. Under the PTO's Written Description Guidelines, there is written description for a generic invention if (1) there is written description for one or more species within that genus, and (2) the species are "representative of the

genus". The examiner has conceded point (1), but contested point (2).

As a result of the present amendments, the claimed genera and subgenera are

(I) Organisms that satisfy the structural (species *Oenococcus oeni*) and functional limitations of claim 1.

(II) Organisms that are within (I) above and further satisfy the process limitations of claim 105.

(III) Organisms that are within (I) and further satisfy the process limitations of claim 107.

We need to separately consider whether the three deposited strains are representative of (I) claim 1, (II) claim 105, or (III) claim 107.

4.3.3. The ultimate test for whether written description is satisfied is whether the disclosure of the application as filed reasonably conveys to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date. Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 USPQ 1111 (Fed. Cir. 1991).

As stated by the Federal Circuit en banc decision in Ariad Pharmaceuticals, Inc. v. Eli Lilly and Co., Case No. 2008-1248, (Slip op, p. 24)(March 22, 2010), "[T]he level of detail required to satisfy the written description requirement varies depending on the nature and scope of the claims and on the complexity and predictability of the relevant technology". Capon v. Eshhar, 418 F.3d 1349, 1357-8 (Fed. Cir. 2005). Relevant considerations include "the existing knowledge in the particular field, the extent and content of the prior art, the maturity of the science or technology, [and] the predictability of the aspect at issue".

The present invention relates to winemaking, which as an art is certainly several thousand years old. Scientific

winemaking may be said to date back to Pasteur's Etude sur les Vin (1866).

The invention also relates, more broadly, to classical microbiology. The selection of mutants for use as fermentation organisms dates back at least to World War I (Clostridium for production of acetone and later butanol; Penicillium for production of citrate; etc.).

As stated by Jose-Luis Barredo, Microbial Processes and Products 2 (2005), "conventionally strain improvement is achieved through random mutation and screening or selecting the so-called classical approach. This empirical method has been practiced for more than 50 yr and has a long history of success (4)". (Exhibit 4).

A brief history of mutation breeding, especially of plants, is provided by Van Harten, Mutation Breeding Theory and Practical Applications 45-47, 51-56, 58-61 (2007) (Exhibit 1). As described by Van Harten, Wolf (1909) and Schiemann (1912) demonstrated that mutations could be artificially (chemically) induced in bacteria and fungi and that these mutations were inheritable. Muller (1927) definitively proved that X-rays could induce mutations in Drosophila and Stadler (1928) irradiated plant seed, with the mutation rate proportional to the radiation dose. The first commercial mutant plant cultivar (of tobacco) was obtained by Tollenaar (1934) and was in commercial use by 1936. An X-ray induced barley mutant with mildew resistance was discussed by Freisleben (1942). Chemical mutagenesis with mustard gas was demonstrated in *Drosophila* (Auerbach 1946) and in barley (Gustaffson 1948). Ethyl methane sulfonate is the most frequently used chemical mutagen in modern plant breeding, and its use dates back at least to 1957 (Westergaard).

With this history, we believe it fair to characterize the present invention as being directed to a mature technology.

We recognize that it may be unpredictable whether a particular radiation or chemical induced mutant of Oenococcus oeni will have the claimed functionality. However, one does not generate one such mutant at a time. Rather one generates hundreds or thousands of mutants simultaneously, and screens them for activity. The experiment may be considered a success if even one of this batch of mutants has the desired activity.

In this regard, we direct the examiner's attention to In re Wands, 858 F.2d 778, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) and Ex parte Chen, 61 USPQ2d 1025 (BPAI 2000). Both cases focused on what could be expected from a single screening experiment, as opposed to an individual candidate (hybridomas in Wands and microinjected embryos in Chen).

4.3.4. In re Ruschig, 3790 F.2d 990 (CCPA 1967) is usually singled out by commenters as the first case to recognize a written description requirement separate from the enablement requirement.

Eight years later, in Feldman v. Aunstrup, 517 F.2d 1351, 186 USPQ 108 (CCPA 1975), the CCPA upheld the BPAI holding that Aunstrup was entitled to priority. The interference count was to a "process for the preparation of a milk-coagulation enzyme which comprises cultivating a milk-coagulation enzyme producing strain of *Mucor miehei* Cooney et Emerson or a natural or artificial variant or mutant thereof…." [emphasis added] Aunstrup's support was a single culture deposit. It is quite clear that a holding of priority necessitated that Aunstrup's disclosure be commensurate with the full scope of the claim, and it had to satisfy not only enablement (which Feldman argued it did not) but also written

description (which the CCPA could have, but did not, raise as an issue).

4.3.5. In discussing what he calls "applicant's argument 4", the examiner concedes that under the holding in Enzo Biochem Inc. v. Gen Probe Inc., 63 USPQ2d 1609 (Fed. Cir. 2002), our deposited strains (like the three Enzo strains enumerated in E Enzo claim 4) enjoy written description (OA, page 7, line 1). (It should be noted that the district court had held otherwise.)

The examiner is correct that in Enzo, the court "expressly declined to rule" that Enzo's broader claims (i.e., not limited to its strains) satisfied written description. However, the district court had granted summary judgment to the effect that the probe claims in question could not, as a matter of law, be "described", and the Federal Circuit reversed and remanded the case to the district court to try the genuine issues of material fact remaining. In other words, the Federal Circuit held that it was possible as a matter of law that the probes "stored" as inserts in the three deposited strains were "representative" of the genera claimed in Enzo's claims 1-6.

Enzo Claims 4 and 6 covered not only the DNA inserts of the three strains, but also subsequences and mutants that satisfied functional limitations. Claim 1 did not even refer to the three deposited strains.

Under the Enzo holding, because our three strains were deposited, their genomes must be considered accessible and sequenceable. 63 USPQ2d at 1616. Likewise, normal strains, such as DSM 7008, (cited at P11, L20) and DSM 15568 (P11, L32) are deposited. Hence, the specification inherently describes the differences which are ascertainable by comparison of the normal strains with the non-citric acid-fermenting strains.

Cp. Invitrogen Corp. v. Clontech Laboratories, Inc., 429 F.3d 1052, 77 USPQ 2d 1161-1176 (Fed. Cir. 2005).

Knowledge in the art as of the priority dates (June 26 and 30, 2003) and international filing date (June 25, 2004) is also relevant. See Capon, supra.

The sequence of the gene encoding the malolactic enzyme (MLE) of Oenococcus oeni (then known as Leuconostoc oenos) was published in 1996. See Labarre, et al. "Cloning and characterization of the genes encoding the malolactic enzyme and the maleate permease of Leuconostoc oenos", Appl. Environ. Microbiol., 62:1274-82 (1996). The protein was purified from L. oenos ML34 by Spettoli, Appl. Environ. Microbiol. 48:900-3 (1984). Both are cited in Exhibit 7.

The cognate sequence for Lactococcus lactis had been published previously. See Ansancy et al., "Cloning, sequence and expression of the gene encoding the malolactic enzyme from Lactococcus lactis", FEBS Lett, 332:74-80 (1993); Denayrolles, et al., "Cloning and sequence analysis of the gene encoding Lactococcus lactis malolactic enzyme: relationships with malic enzymes", FEMS Microbiol. Lett., 116:79-86 (1994). Both are cited in Exhibit 7.

The relationship of the O.oeni enzyme to homologous enzymes of other lactic acid bacteria was known by phylogenetic analysis based on partial malolactic enzyme gene sequences. See Groisillier and Lonvaud-Funel, Int. J. System Bacteriol., 49:1417-28 (1999) (Exhibit 7).

Once the complete genome of O. oeni was sequenced (published in 2005, adonittedly after the PCT filing date, but arguably within the skill of the art in 2004), "genes related to flavor modification in wine, such as malolactic fermentation capacity and citrate utilization were readily identified". Abstract, Mills, et al., "Genomic analysis of

Oenococcus oeni PSU-1 and its relevance to Winemaking, FEMS Microbiol. Rev. 29(3):465-75 (August 2005) (Exhibit 8).

Claim 1, as presently amended, is directed to strains of a single species (*Oenococcus oeni*) and the natural variation among strains of that species would have been expected, as of the relevant dates, to be small.

According to Ze-Ze and Tenreiro, "The Oenococcus oeni genome: physical and genetic mapping of strain GM and comparison with the genome, of a 'divergent strain PSU1", Microbiology, 146 (Pt. 2) 3195-3204 (December 2000) (Ex. 9), restriction mapping did not reveal any major genomic rearrangements. "The genomic conservation... suggests homogeneity within the species, which was not unexpected in view of the restricted ecological niche of O. oeni"[2].

Likewise, we would expect that the nature of the mutations that would convert a normal strain into a strain that preferentially ferments malic acid rather citric acid into lactic acid is constrained. Hence, the deposited strains are representative of the limited subset of O. oeni strains with the recited properties.

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[2] In post-filing literature, there is some disagreement as to the degree of interstrain variability. On the one hand, Lechiancol, et al., "Evaulation of intra-specific diversities in Oenococcus oeni through analysis of genomic and expressed DNA", Systematic & Appl. Microbiol., 29(5):375-81 (July 2006) (abstract only, Exhibit 10) says that "several studies have demonstrated that O. Oeni is a quite homogeneous species and strains are difficult to differentiate especially when isolates from the same region are analyzed". On the other hand, Marcobal, et al., "Role of hypermutability in the Evolution of the Genus Oenococcus", J. Bacteriol., 190(2):564-70 (2008) (exhibit 11) admitted that the initial impression (citing five references) was that "the species is quite homogeneous", but reviewed evidence of allelic variation in the post-filing Rivas, Appl. & Environ. Microbiol., 70(12):7210-19 (December 2004) (Abstract attached as Exhibit 12) paper, and of an impaired mismatch repair system in strain PSU-1 according to a 2006 paper. We believe that these post-filing reports are legally irrelevant to the determination of whether the reduced-to-practice strains are representative of the claimed subject matter.

4.3.6. In connection with what the examiner refers to as applicants' arguments 2 and 3, the examiner concedes that the cases cited by the examiner are related to DNA or protein claim, but urges that the court (at least in Fiers) intended its reasoning to apply to products in general. The examiner urged that it would apply to cells.

However, in Amgen II[3] (the terms "vertebrate cell" and "mammalian cell" were deemed to be meaningful even in the absence of a specific DNA sequence.

We do not contend that the written description requirement, in general terms, only applies to DNA or protein claims. Rather, what we are saying is that even if the cited cases indicate that disclosure of a sequence is necessary for written description of a DNA or protein[4], they do not hold it necessary for written description of a cell.

4.3.7. A comparison to written description practice with respect to antibody technology may be helpful. In the PTO's own Written Description Training Materials (Revision 1, March 25, 2008), Example 13, a claim to "an isolated antibody capable of binding to antigen X" has written description if antigen X is adequately described, because methods of making antibodies are conventional[5]. The PTO observed that "It does not appear that persons of skill in the art consider knowledge of the amino acid sequence of the variable regions critical for the purposes of assessing possession of an antibody".

We respectfully submit that microbiologists isolated mutants well before methods of DNA or protein sequencing were

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[3] Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 65 USPQ2d 1385 (Fed. Cir. 2003).

[4] And Capon v. Eshhar, supra and Enzo Biochem, supra, both held that sequence disclosure is not always necessary even in that context.

[5] This Example was possibly influenced by Staehelin v. Secher, 24 USPQ2d 1513 (BPAI 1992) and Noelle v. Lederman, 355 F.3d 1343, 69 USPQ2d 1508 (Fed. Cir. 2004).

known and hence it's clear that knowledge of the mutated sequence(s) was not considered critical for purposes of assessing possession of a mutant microbial strain obtained by radiation or chemical treatment.

O. oeni is a well-established species, and the properties of *O. oeni* are well known, and defined in e.g., Bergey's Manual[6]. Hence, it is analogous to the known antigen of the example.

While the methods of mutating strains differ from those of raising monoclonal antibodies, the reference (normal) strains of O. oeni serve as the target for mutation just as the reference antigen serves as a target for antibody binding.

In our case, a large number of mutant strains are screened for the desired metabolic activity, just as in the immunological case, a large number of hybridomas are screened for secretion of antibodies with the desired binding activity.

The disclosure of the species (*O. oeni*) from which to derive the mutants, and of the assay, with the three deposited strains stands as proof that the process is efficacious, and establishes possession of the subject matter of claim 1.

4.3.8. Another useful comparison is with respect to enzyme technology. In the Interim Written Description Guidelines (June 9, 1998), the PTO suggested that a claim to "an isolated mutanase enzyme produced by Bacillus, defined by various ranged physicochemical properties, and supported by 3 disclosed Bacillus mutanases, was "described" even though no sequences were set forth. It was held that the skilled worker

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[6] O. oeni was formerly named Leuconostoc oenos, and it so appears in Bergey's Manual of Determinative Bacteriology (8th ed., 1974) page 513 (Exhibit 5). The proposal to reclassify it was made in Dicks et al., "Proposal to Reclassify Leuiconostoc oenos as Oenococcus oeni", Int. J. Determin. Bacteriol., 45(2):395-7 (1995) (Exhibit 6).

could "reasonably identify" other members of the claimed genus.

Here, the claimed strains are characterized by both explicit properties and the morphological, metabolic and genetic characteristics implicit in designating them as being of the species *O. oeni*. They are, in the words of Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd., 18 USPQ 2d 1016 (Fed. Cir. 1991), "like a chemical defined by its physical or chemical properties… sufficiently [to] distinguish it".

4.3.9. Claim 105, as amended, is limited to organisms "selected from the group consisting of DSM 15569, DSM 15570, DSM 15571, and mutants derived directly or indirectly therefrom by mutation and selection".

Mutations may fall into four categories: (a) mutations made outside genes, which have no phenotypic effect; (b) mutations which are in genes but, by virtue of redundancy of the genetic code, are "silent"; (c) non-silent mutations which are in genes, but not genes involved in malolactic metabolism; and (d) non-silent mutations which are in such genes. Only (d) mutations specifically affect the claimed activity, although (b) or (c) mutations could be lethal to the organism.

DSM 15569, DSM 15570 and DSM 15571 already have the desired activity and hence most mutants thereof would be expected to retain the activity. Hence, a mutate-and-screen experiment using one of these strains as a starting strain would be even more likely to produce at least one mutant strain with the claimed activity than an experiment beginning with a "normal" O. oeni strain.

Claim 105, moreover by virtue of its process limitations falls into a "safe haven" for product-by-process claims.

The Eli Lilly interpretation of written description developed out of case law relating to conception. In Amgen,

Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) it was held that Fritsch (alleged prior inventor of DNA sequences encoding human erythropoietin) could not have conceived of this DNA until he had a mental picture of its structure (sequence). The court explained that "Conception does not occur unless one has a mental picture of the structure of the chemical, or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics are sufficiently distinguish it". ID. 1021 [emphasis added].

This doctrinal point was transported from "conception" to "written description" by Fiers v. Sugano, 984 F.2d 1164, 1169, 25 USPQ2d 1601, 1604-5 (Fed. Cir. 1993):

> Our statement in *Amgen* that conception may occur, *inter alia*, when one is able to define a chemical by its method of preparation requires that the DNA be claimed by its method of preparation. We recognized that, in addition to being claimable by structure or physical properties, a chemical material can be claimed by means of a process. A product-by-process claim normally is an after-the-fact definition, used after one has obtained a material by a particular process. Before reduction to practice, conception only of a process for making a substance, without a conception of a structural or equivalent definition of that substance, can at most constitute a conception of the substance claimed as a process. Conception of a substance claimed *per se* without reference to a process requires conception of its structure, name, formula, or definitive chemical or physical properties.

Claim 105 is plainly entitled to the safe haven accorded to a product-by-process claim.

4.3.10. Claim 107 is directed to the organism of claim 1 when obtained (1) by a particular process, or (2) by further mutation of an organism obtained by the process of (1).

We think it useful to point out that we believe that the critical discovery was that it was in fact possible to mutate *O. oeni* to substantially block citric acid degradation without impairing malolactic fermentation. Once applicant made that information public by filing the present application, it enabled competitors to find their own strains by the methodology disclosed by applicants.

Claim 107, like 105, is a product-by-process claim, and the process steps are enumerated by 107 in greater detail than for 105. Hence, it too is entitled to the Amgen-Fiers safe haven.

4.3.11. The written description rejection has been applied, not only to the organism claims, but also to the following method-of-use claims: 16, 18-20, 22-26, 29, 31-32, 34-35, 37-38, 40-42, 55, 58-59, 94, 95, 98-100. However, this written description rejection was not applied to method-of-making claims 50-52.

The close relationship between claims 50-52 and claim 107 (and 110) should be apparent, and we respectfully submit that the same considerations that led the examiner to treat claims 50-52 differently should also apply to 107 and 110.

Since claim 50 has been rewritten in independent form, we believe the examiner is free to deem 50 and dependent claims 51, 52, and 112-115 to be allowable.

We are willing to discuss the possibility of cancelling and/or converting organism claims to process claims dependent on claim 50 or product-by-process claims dependent on claim 107 if that would result in allowance.

4.3.12. The Examiner has taken the position that since Applicant has not characterized the precise genetic nature of the mutations in the parental strain that characterize the deposited strains, Applicant should be limited to those strains.

Were this view of written description to prevail, patents on novel organisms obtained by random mutation and selection, or spontaneous mutants isolated from nature, would be commercially worthless, as the protection limited to the deposited strain would be easily evaded as competitors ordered deposited strains shipped by the IDA to a location outside the USA, further mutated it there, and then used the further mutated strain in the USA with impunity[7].

Alternatively the competitors could make mutants, even in the USA, of a non-infringing parental strain, and screen (using the disclosed screening assay) for mutants with the same functionality.

Inventors and their companies would then learn to keep such organisms as trade secrets rather than enriching the art by depositing the organisms and describing their characteristics.

The examiner responds, "regarding argument 1, applicant's opinion on the utility of the patent system and the ways to skirt patent protection are interesting; however, they are an argument with regard to whether there should be a written description requirement and are not relevant to whether or not the written description requirement has been met".

We respectfully disagree. These policy considerations affect not merely whether there should be any written

[7] Claim 105, if allowed, does cover mutants of the deposited strains.

description requirement, but also how that requirement is interpreted.

The examiner adds, "It is of note that applicant's means of skirting patent protection (taking strains owned by another and mutating them in order to obtain their own strain) is precisely the manner in which applicant disclose to obtain the current invention".

The examiner appears to have overlooked the difference between what applicant did and what applicant fears others will do. Applicant took a strain (not patented, by the way) that degraded citric acid during malolactic fermentation (with the disadvantages set forth on P21, L6-25); and derived a materially improved strain that ferments malic acid to essential completion without the problem of extensive degradation of citric acid.

What applicant fears is that others will derive mutants from applicant's strains, or from normal strains, that have the same useful properties as those of applicants, based on applicant's guidance. The purpose of the patent system is to encourage innovation by a grant of exclusivity commensurate with the applicants' teachings. If applicant is given

protection only of the deposited strains, it provides an unjust windfall to applicant's competitors.

Respectfully submitted,

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Enclosures
-Exhibit 1 Van Harten, Mutation Breeding Theory and Practical Application pp. 45-47, 51-56, 58-61
-Exhibit 2 "concentration" from Condensed Chemical Dictionary
-Exhibit 3 "Concentration Scales" from McGraw-Hill Encyclopedia of Science and Technology
-Exhibit 4 Barredo, Microbial Processes and Product (2005), page 2
-Exhibit 5 Bergey's manual of Determinative Bacteriology (8th ed. 1974) pp. 510-513
-Exhibit 6 Dicks, et al (1995).
-Exhibit 7 Groisillier and Lonvaud-Funel (1999)
-Exhibit 8 Mills (2005)
-Exhibit 9 Ze-Ze (2000)
-Exhibit 10 Lechiancole (2006)
-Exhibit 11 Marcobal (2008)
-Exhibit 12 Rivas (2004)

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